AMERICAN JOURNAL OF PHARMACY

and

THE SCIENCES SUPPORTING PUBLIC HEALTH

SINCE
1825

IN MEMORIAM
SAMUEL L. HILTON

FEBRUARY
1944

● Since the introduction of Prontosil—the first sulfanilamide compound—a successive series of life-saving "sulfa" drugs has been offered to the medical profession.

With pleasure we announce the addition of SULFADIAZINE to the distinguished selection of chemotherapeutic agents already supplied by Winthrop.

Prices through wholesale druggists are as follows:

Tablets of 0.5 Gm.

Bottles of 50	.....per bottle	$ .87
Bottles of 100	.....per bottle	1.56
Bottles of 500	.....per bottle	7.50
Bottles of 1000	.....per bottle	14.40

Winthrop Chemical Company, Inc.
170 VARICK STREET
NEW YORK 13, N. Y.

PHARMACEUTICALS OF MERIT FOR THE PHYSICIAN

927B

This advertisement appearing in leading Drug Journals.

Physicians Prescribe Drugs,

NOT DISCOUNTS

No substantial prescription business ever was built on a discount basis. Heavy buying of medicinal agents for the sake of extra discounts usually results in overstocks which leave an assortment of odds and ends that nobody wants at any price. Profits are made in selling, not in buying. Unwanted merchandise is always a liability, even if it costs nothing at all. Selection of prescription stocks should be governed by one factor only—the prescribing habits of physicians. To the physician belongs the right to diagnose and prescribe, to the pharmacist the right to compound and dispense. Physicians favor pharmacies where the Lilly Label predominates.

Young in years, old in experience, is R. A. Gibson, who joined the Lilly organization twenty-two years ago last October. Mr. Gibson lives with his wife and six children in Washington, Pennsylvania, where he accepted his first assignment in January, 1921.

WE PAY HIM · BUT HE WORKS FOR YOU ·

ELI LILLY AND COMPANY, INDIANAPOLIS 6, INDIANA, U. S. A.

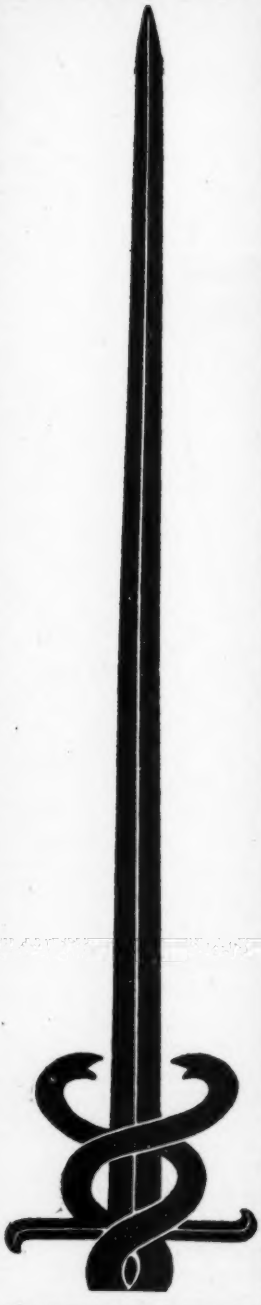
SCRAPEY THROATS are at their peak . . . and so are sales of 'S. T. 37' Antiseptic Solution. By recommending the large 12-oz. size, you assure yourself a profit of at least 33⅓% on your investment! Stock up on this exceptional antiseptic solution and recommend it with confidence.

'S. T. 37' Antiseptic Solution is a preparation that offers not only high *germicidal action* but also exceptional nontoxic features. Pathogenic bacteria are rapidly destroyed by 'S. T. 37' Antiseptic Solution. Inflamed mucous tissues and open wounds are soothed by its analgesic effect. Normal bleeding is not hindered. 'S. T. 37' Antiseptic Solution also has this important characteristic: a low surface tension which facilitates *penetration of minute tissue spaces.* It is bactericidal and is vigorously carried into narrow tissue crevices and fissures.

Colorless, odorless, readily miscible in water, 'S. T. 37' Antiseptic Solution is an exceptionally useful antiseptic for general use. It contains no heavy metals such as mercury and is harmless even if swallowed accidentally in full strength.

'S. T. 37' Antiseptic Solution is supplied in bottles of five and twelve fluid-ounces. **Sharp & Dohme, Phila. 1, Pa.**

'S. T. 37' *Antiseptic Solution*

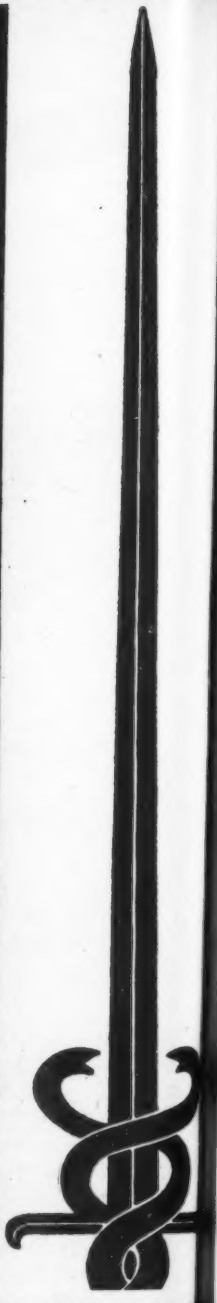


ENLIST TODAY in the fight AGAINST CANCER

160,000 Americans die of cancer annually. Authorities say *many of these deaths could be avoided.*

Help us spread the knowledge that *cancer can, in many cases, be cured.* Enlist today in your local unit of the Women's Field Army.

In the Metropolitan Area, address the
New York City Cancer Committee
130 East 66th Street



AMERICAN SOCIETY FOR THE CONTROL OF CANC

350 MADISON AVENUE, NEW YORK CITY

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 116. FEBRUARY, 1944 No. 2

CONTENTS

Published monthly by the Philadelphia College of Pharmacy and Science 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $3.00 — Foreign Postage, 25 Cents Extra

Single Numbers, 30 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter at the Post Office at Philadelphia, Pa. Under Act of March 3, 1879

Acceptance for Mailing at Special Rate of Postage Provided for in Section 1103 Act of October 3, 1917. Authorized February 15, 1920

IN MEMORIAM

SAMUEL L. HILTON

THE word which came a few days ago of the death on January 30, 1944 of Samuel L. Hilton of Washington, D. C., brought a realization once more, to those who have known the truly great pioneer leaders of American pharmacy, that a generation of giants was rapidly passing.

Dr. Hilton was first and always a practicing pharmacist. Through several generations of doctors and patients in Washington, his prescription department and his pharmaceutical laboratory at 22nd and L Streets, N. W. was a centre of unusually able professional service. Doctors came to him for advice on the latest drugs and their combination, some sent him analytical work and others bought sterile products which early became his specialty.

He pioneered in the preparation and neutralization of sterile solutions of Salvarsan and frequently accompanied a physician to the home of a patient to assist in its administration. His quite extensive line of injectable sterile products in ampuls, which he personally prepared and sterlized were widely used in Washington before the larger pharmaceutical firms even offered such products.

He was proud of the record of having supplied medicines to, and counted as personal friends a number of, the occupants of the White House as well as Congressmen, judges, theatrical celebrities any many others prominent in the nation's capital.

However, Dr. Hilton did not permit the duties of a busy pharmacy to interfere with his broader interests and services to his profession and he actively participated in many outside fields.

At the 1940 Pharmacopœial Convention he told of having been present at each U. S. P. Decennial Convention since 1880, although at that time he was only a boy of fifteen. His Pharmacopœial associations continued throughout his life. For four decades from 1900, he was Chairman of the U. S. P. Convention Arrangements Committee and in that capacity he took an active and influential part in

the conduct of the Conventions. For twenty-eight years he served as Treasurer of the U. S. P. Convention, retiring in 1940.

Dr. Hilton's interest in the American Pharmaceutical Association was equally great. He was the A. Ph. A. Treasurer for many years and also a most efficient Chairman of the Council over a long period, guiding its affairs wisely and forcefully. His intimate knowledge of Washington and his wide acquaintanceship among officials was no small factor in securing the splendid location for the A. Ph. A. Headquarters Building. For years he went daily to the Washington office to give advice on the Association's problems and affairs. The Association properly honored him with its Presidency in 1921. Dr. Hilton also served the A. Ph. A. as an active member of the National Formulary Committee and in this office as in every other duty he assumed, he took an active part and conducted many practical experiments in the laboratory of his pharmacy.

He graduated from the National College of Pharmacy in 1880 and always took an interest in its affairs, not only as a teacher and special lecturer, but also a member of the Board of Trustees until its merger with George Washington University.

As one of the leaders of the early A. Ph. A. policies he advised and helped bring about the establishment of an independent business association for pharmacy, to handle trade matters which were then believed incompatible with the highly professional ideals of the A. Ph. A. and he thus became one of the founders of the National Association of Retail Druggists.

This brief outline cannot begin to do justice to so splendid a pharmacist as Samuel L. Hilton. Few have given unselfishly so varied, efficient, and enthusiastic a service to their profession. Through his unwavering honesty, his loyalty to his friends and to pharmacy, and his driving sense of duty he has built an enduring monument. The award of the Remington Medal, in 1935, a recognition of these qualities, was a fitting tribute to his many sterling attributes.

E. Fullerton Cook.

E D I T O R I A L

ONLY POSITIVE ACTION CAN AVERT GOVERNMENT CONTROL

IN a previous issue of this journal we entered our opposition to the Murray-Wagner-Dingell Bill and its provisions for the bureaucratic control of medicine but this does not mean that we feel that the present or past status of medical care in this country is at all adequate or that it even approaches the ideal. It is simply that we do not have faith in government operation of anything as personal and vital as the relationship between a person and those in whom he places the responsibility for safeguarding his health and even his life. Such relationships should be as inviolable as our marital choice since they affect us just as profoundly and should be as carefully safeguarded.

To stop here is, however, to court disaster. We in the professions related to public health cannot afford to sit complacently and parry the criticism of those who quite properly ask "Can not some real improvement be made in raising the standards of health of the common man?" It is ridiculous for any well-informed person to take the position that medical care in its present state of organization is adequate for all income groups. This does not answer the question satisfactorily nor does it offer any effective barrier to the serious consideration of bills like that now before Congress. At best the public health professions can muster only a few hundred thousand negative votes on the basis of objections without something better to offer. Labor is well aware of the several weaknesses in the present system and their supporters can easily overwhelm such feeble efforts as those so far expended. Let no one believe that the private practice of medicine, pharmacy, dentistry or anything else is a divine right. It, is, rather, a privilege granted by society which it serves but only so long as it concerns itself primarily with the protection and assistance of society as a whole. What has been given can likewise be taken away.

There are two things that must be done if real progress without government control is to be achieved. First and foremost there must be active cooperation between medicine, dentistry and pharmacy. This has never been an accomplished fact. We, like medicine, have

managed to get along without such cooperation. Our progress has not been as easy nor our recognition as great but now by the same token we do not have as much to lose by letting things take their natural course. There will always be a demand for drugs under any system of medical care but under government control the current practice of medicine will be almost unrecognizable. We in pharmacy have always wanted and vitally needed the support of organized medicine. We still need it. Medicine, however, now stands at a cross-roads since either we all work together with mutual trust and respect or even organized medicine may find itself hopelessly enmeshed with government. The pharmacist is not to be overlooked in his influence on public opinion and it should be remembered that the general public rarely reads the *Journal of the American Medical Association*. In public meetings on medical care organized medicine consistently seems to emerge only second best with the result that the trend toward government control seems greater day by day.

With the bona fide cooperation of the health professions their first objective should be to offer a plan of health insurance to the American people which still safeguards private enterprise but accomplishes what millions of Americans now demand—a means of taking care of the various emergencies that arise throughout life due to sickness and injury. We should solicit the aid of the great insurance institutions of the country and also that of American industry since both are profoundly concerned. Insurance companies are already uneasy about the increasing participation of the government in insurance and industry would willingly participate in the cost of such insurance since if it does not it will pay even more through taxation.

With a finished plan the health professions, insurance and American industry can then say to the people "Here is a better health insurance plan; it gives you what you have asked for and in addition it avoids regimentation and bureaucratic control. It is the real American way." Then and then only can we properly and effectively oppose government conceived plans, by ourselves offering something better. We must not overlook the fact that it is the function of government to protect its citizens in the absence of some other private agency which does so to the satisfaction of the majority concerned. There has never been a time in history when a strictly reactionary policy was successful. To avoid the pitfalls of government control we must take positive action.

L. F. Tice

CETYLPYRIDINIUM CHLORIDE *

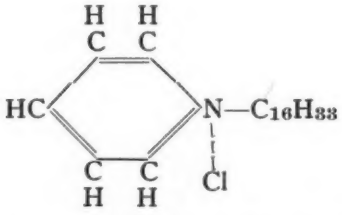
By C. Lee Huyck, Ph. D.

Introduction

As early as 1916 Jacobs and his coworkers (1, 2, 3) at the Rockefeller Institute reported the results of a systematic study of synthetic germicides. They pointed out that quaternary ammonium salts have definite germicidal action. Until recently this type of compound has been very little investigated.

Physical Properties

Cetylpyridinium chloride is an antiseptic of high germicidal and bacteriostatic potency. Its chemical structure is:



It is freely soluble in water, forming a clear colorless solution. It is soluble in acetone and in alcohol but insoluble in ether and only slightly soluble in benzol. The aqueous solution is slightly acid to litmus and possesses a slight aromatic odor. The 1:1000 aqueous solution has an astringent taste which gradually disappears on dilution. When shaken, aqueous solutions foam like soap solutions because of their low surface tension.

The surface tension of aqueous isotonic solutions has been determined by the ring tensiometer method at 24.5° C. with the following results:

1:1000 Cetylpyridinium chloride	40.8 dynes/sq. cm.
1:5000 Cetylpyridinium chloride	45 dynes/sq. cm.
1:10,000 Cetylpyridinium chloride	51 dynes/sq. cm.
Distilled Water	71.2 dynes/sq. cm.

* Ceepryn brand of cetylpyridinium chloride, manufactured by The Wm. S. Merrell Company, Cincinnati, Ohio.

Cetylpyridinium chloride may be considered as an invert soap differing from ordinary soap in containing no metallic base and in being chemically reversed in respect to the electrical charges of the groups in the molecule. Like other surface active detergents cetylpyridinium chloride reduces the angle of contact between water and the material wetted resulting in a greater capillary activity than water. It reduces the surface tension of water and lowers the interfacial tension between water and the other surfaces contacted such as solids and liquids making it desirable in wetting the skin and penetrating the tissue.

Compatibilities and Incompatibilities

A 0.5 per cent solution in a solvent containing 50 per cent alcohol and 10 per cent acetone is compatible with ephedrine hydrochloride, diothane hydrochloride, picric acid, sulfathiazole, sulfanilamide, benzocaine, procaine hydrochloride, cocaine hydrochloride in 1 per cent concentrations. Benzyl alcohol, glucose and 1:1000 adrenalin chloride solutions are compatible in 10 per cent concentration while monethanolamine, diethanolamine, triethanolamine, triacetin, and commercial sorbitol are compatible in 3 per cent concentrations. Exsiccated alum, gelatin and tannic acid are incompatible with this solution in 1 per cent concentrations while Burow's solution is incompatible in 10 per cent concentrations. Berberine phosphate and acriflavine hydrochloride are compatible to the extent of 0.2 per cent and 0.05 per cent respectively.

The one-tenth per cent aqueous solution is compatible with urea, with 1:1000 solution adrenalin chloride solution and with glucose in 10 per cent concentrations as well as with 5 per cent chloral hydrate and 0.5 per cent allantoin. It is compatible with procaine hydrochloride, cocaine hydrochloride ephedrine hydrochloride, thiourea, and gelatin in 1 per cent concentrations. Sulfathiazole, sulfanilamide, benzocaine, exsiccated alum, diothane hydrochloride, tannic acid, picric acid are incompatible in 1 per cent concentrations; 5 per cent resorcinol monoacetate and 50 per cent Burow's Solution are also incompatible. Recently Powney (4) reported that a precipitate is formed when an aqueous solution of sodium hexametaphosphate is added to an aqueous solution of cetylpyridinium bromide.

Mode of Action

According to the accepted theory of the detergency of wetting agents (5) cetylpyridinium chloride has both hydrophilic and lipophilic properties; the hydrophilic properties originate from the chloride anion which is attracted to the water while the lipophilic properties originate from the cetylpyridinium cation which is attracted to lipoids. Generally, the higher the molecular weight of the hydrocarbon residue, the stronger is the lipophilic property of the substance. When it is placed in contact with water and lipoids a definite orientation of the two phases takes place which establishes contact with both types of matter and with its low surface tension is responsible for its high tissue penetrating action. When applied to the soiled surface of the skin an emulsion of soiled particles is formed while cleansing takes place as a result of replacement of the emulsified soiled particles by excess of wetting agent.

Frobisher (6) found that surface tension is an important factor in bacterial growth, morphology, cell division and to a lesser extent in the motility of bacteria as well as their ability to retain Gram's stain. The loss of virulence of pneumococci after treatment with surface tension reducents may be due to the fact that these bacteria disintegrate when they are subjected to low surface tension and the dissolution of pneumococci by bile may be due to the low surface tension induced by this substance.

Baker and coworkers (7) studied the action of synthetic detergents on the metabolism of bacteria and concluded that all the cationic detergents studied are very effective inhibitors of bacterial metabolism at 1:3000 concentration while several are equally active at 1:30,000. Few of the anionic detergents inhibit the metabolism as effectively as the cationic compounds. Gram positive and Gram negative microorganisms are equally sensitive to the action of the cationic detergents. The inhibitory action on both types of detergents is influenced markedly by the hydrogen ion concentration. Studies of homologous series of straight chain alkyl radicals showed that maximum inhibition is exerted by lauryl, myristyl and cetyl radicals. Cationic detergents exhibit an inhibitory activity comparable to noncationic quaternary ammonium compounds. Certain anionic detergents stimulate bacterial metabolism in ionic concentrations.

Albert (8) has reviewed the methods by which various types of antiseptics kill bacteria. Cationic germicidal wetting agents of which

cetylpyridinium chloride is an example contain basic ions or cations which interact with the acid groups of the bacteria to form feebly ionized compounds.

The Relationship of Chemical Constitution to Germicidal Action

Shelton and coworkers (9) correlated the structure and germicidal activity of certain acyclic quaternary ammonium salts. In testing the effect of the chain length of the alkyl group on the germicidal activity of alkylpyridinium chlorides, they found that the germicidal activity increased rapidly from an alkyl group containing eight carbon aroms to an alkyl group containing sixteen carbon atoms. With alkyl radicals containing more than sixteen carbon atoms the germicidal activity gradually decreased. In testing the effect of various halogen anions of cetylpyridinium halides for germicidal activity, the chloride was slightly more active than the bromide and the bromide was more active than the iodide. Also, the sulfate anion was not quite as germicidal as the chloride anion. The organic anions such as the acetate, benzoate, and salicylate were active germicides but they were less active than the inorganic anions.

Shelton et al. (10) extended their work on the correlation of structure and germicidal activity of some quaternary ammonium salts by reporting on compounds derived from cyclic amines. Pyridine, picoline, lutidine, quinoline, piperidine, pipecoline and methyl morpholine were the cyclic amines tested. The maximum bactericidal activity was produced by the pyridine derivative, cetylpyridinium chloride. The cetyl amines derived from morpholine and piperidine had little germicidal action, but the quaternary salts obtained from the N-methyl amines were strongly germicidal. N-cetyl-N-methyl piperidinium bromide was equal to cetylpyridinium chloride in bactericidal activity, followed in decreasing order by the quinolinium salt and the N-methyl morpholinium salt. It was concluded that the compounds having the simplest structure about the nitrogen atom had the highest germicidal activity. Generally, C-alkylation of the cyclic amine nucleus reduced the germicidal activity, and in the same way an increase in the molecular weight of the cyclic amine had a negative effect. The presence of oxygen in the molecule decreased the activity as suggested by the inactivity of the morpholinium salt as compared to the piperidinium salt.

Bacteriological Action

Blubaugh and coworkers (11) found that both the tincture and the aqueous solution of cetylpyridinium chloride were highly germicidal for virulent organisms in the presence and absence of organic matter when tested by the F. D. A. technique. Germicidal activity was determined for several species of pathogenic and non-pathogenic organisms. The bactericidal properties of this compound compared favorably with those of other well known germicides of the mercurial, phenolic and halogenous types.

Miller and Baker (12) reported on the comparative effects of a number of anionic and cationic detergents on the metabolism of gram positive and gram negative bacteria. They found the anionic detergents inhibited the metabolism of gram positive bacteria without having any significant effect on the gram negative organisms. On the contrary, the cationic detergents inhibited the metabolism of both the gram positive and gram negative bacteria to the same degree.

Blubaugh et al. (13) continued the study of the germicidal activity of cetylpyridinium chloride on various organisms by the F. D. A. method and compared the results with a series of well known germicides. Test for bacteriostatic activity demonstrated no inhibition in the case of vegetable cells but on the contrary the results indicated that for periods in excess of 24 hours, the action was bactericidal rather than bacteriostatic. Tests for killing time showed that a 1 :4000 dilution of the compound was bactericidal for vegetable cells in less than 15 seconds.

Gershenfeld and Milanick (14) examined wetting agents and surface tension depressants for germicidal activity. They found the germicidal activity of both anionic and cationic types of compounds were markedly influenced by hydrogen ion concentration.

Green and Birkeland (15) tested the germicidal activity of cetylpyridinium chloride on the more common spores by the F. D. A. technique in liquid media and on contaminated instruments. The results indicated that cetylpyridinium chloride was an effective and practical germicide for the more common bacterial spores.

Clarke (16) made a bacteriological comparison of cetylpyridinium chloride with other sterilizing agents. No skin reaction followed its use. Scratch and patch tests of the 1 :200 tincture and an equeous solution were negative at the end of twenty-four and forty-eight hours as well as seven days.

Ordal and Borg (17) found that the lactic dehydrogenase of *Staphylococcus aureus* was inhibited by 1.7×10^{-5} M. cetylpyridinium chloride. A concentration of 1.1×10^{-3} M. cetylpyridinium chloride was required to inhibit the lactic dehydrogenase of *Escherichia coli.* Both cationic and anionic wetting agents inhibited the oxidation of lactate solutions by *Staphylococcus aureus* but only the cationic agent inhibited the oxidation of lactate solution by *Escherichia coli.*

Koloff and coworkers (18) tested a group of twenty-seven alkyl-pyridinium and alkyl-picolinium halides. Preliminary germicidal tests were made to discover any increase in activity due to the introduction of a methyl radical into the aromatic nucleus of these quaternary compounds. Although each of the products of the group showed definite germicidal activity, the introduction of the methyl group was not accompanied by any significant increase in activity. The authors reported that a 1:50,000 aqueous solution of cetylpyridinium chloride killed *Staphylococcus aureus* in ten minutes at 37° C. but not in five minutes when tested by the F. D. A. method.

Reed et al. (19) reported on the germicidal activity of cetylpyridinium chloride on various organisms at 20° C. by the F. D. A. method and compared the results with previous findings on the same group of organisms at 37° C. Variation in results at the two temperatures were apparently not due to pathogenicity, morphology or resistance to phenol. Temperature curves were established for four types of germicides: a mercurial, a quaternary ammonium salt, a halogen and phenol.

Blubaugh et al. (20) used the F. D. A. technique in testing aqueous cetylpyridinium chloride in the presence of serum and concluded that this germicide was highly bactericidal for several species of pathogenic and non-pathogenic organisms. The optimum pH for cetylpyridinium chloride was in the range of 6 to 8 while the average pH of the aqueous solution is 7.3.

Pharmacological Action

In testing cetylpyridinium chloride pharmacologically, Warren and coworkers (21) found a 1:3000 solution slightly irritating to the conjuctival mucous membrance but not to the skin. When injected intravenously in rabbits the M. L. D. was 20 mg./kg. It was more toxic when given intraperitoneally. Given by mouth 400 mg./kg. killed one rabbit in six. Daily oral administration of smaller doses

to rabbits for five weeks caused no significant damage. The toxic manifestations were curare-like action with central stimulation and peripheral paralysis.

Sarber (22) compared the effectiveness of cetylpyridinium chloride with sodium ethylmercurythiosalicylate and hexylresorcinol. He showed that cetylpyridinium chloride had the highest relative efficiency of the three germicides tested. Sodium ethylmercurythiosalicylate and hexylresorcinol followed in effectiveness in the order given. The author advanced evidence to support the theory that the skin has a definite bactericidal power which it may exert if it is not injured by chemicals. With germicides of low toxicity like cetylpyridinium chloride the combined action of the two agents overcome bacterial invasion which neither the skin alone nor the germicides is able to overcome by itself.

Green and Birkeland (23) determined the effect of phenol, iodine and cetylpyridinium chloride solutions on experimental *Staphylococcus aureus* infections of the chorio-allantoic membrane of chick embryos. Cetylpyridinium chloride definitely reduced the degree of infection. Phenol and iodine solutions had no appreciable effect.

Disinfecting Action

In a brief review of quaternary compounds used as disinfectants, Wakelin (24) pointed out that the cetyl radical was instrumental in rendering these compounds surface active making them good wetting agents. Quaternary compounds containing sulfur are well known in Great Britain as disinfecting and preserving agents for preparations containing sugar, starch and protein. A nutrient gelatin mixture containing dextrose preserved with 0.05 per cent of a quaternary compound containing sulfur did not decompose after ninety days.

Cetyltrimethylammonium bromide which is a compound closely related to cetylpyridinium chloride was reported by Shelton et al. (9) and by Barnes (25) to be an excellent disinfecting and cleansing agent. It was able to materially reduce the number of bacteria on normal skin and to completely sterilize dirty bowls. A 1 per cent aqueous solution was neutral and felt soapy to the touch but was not painful when applied to abrasions of the skin.

Williams and coworkers (26) recently investigated the cleansing and sterilizing properties of a 1 per cent aqueous solution of cetyltrimethylammonium bromide. It has considerable antiseptic power

when applied to wounds and the skin surrounding wounds. It cleanses and sterilizes instruments. It is also highly effective in removing dirt and bacteria from the hands and is an admirable solution to apply to the hands of surgeons in gloveless surgery. Skin reactions occurred in a small number of cases but it was found that the chemically related detergent cetylpyridinium bromide was less likely to induce these reactions.

Action in the Mouth

In searching for a compound which can effectively inhibit the metabolism of microorganisms found in the lesions of dental caries or in plaques associated with such lesions, Miller et al. (27) studied the action of the quaternary ammonium type wetting agent described by Domagk (28) on the metabolism of bacteria associated with dental caries. The inhibition of the metabolism of the so-called dental bacteria was greater than the inhibition of metabolism obtained by Miller (29) for fluoride or iodoacetate. Because of the unusual inhibitory action of the quaternary ammonium compound and its excellent power of penetration and cleansing, as well as its low toxicity for the mucous membranes, the authors concluded that it deserved further study.

In looking for a non-toxic compound possessing the property of rapid penetration of the dense mass surrounding the teeth, Miller and coworkers (30) tested the inhibitory effect of the quaternary ammonium synthetic detergent described by Domagk (28). This compound reduced the surface tension of water in very low concentrations and it acted as a wetting and cleansing agent. Besides suppressing very effectively aerobic glycolysis of plaque material, it prevented any significant decrease in pH of this material. *In vivo,* the results demonstrated that the lactic acid bacteria were completely suppressed. In view of the present state of knowledge of dental caries, however, no definite conclusions concerning the prevention or treatment of dental caries can be drawn from this work. The efficacy of any agent or procedure proposed for the cure, prevention, or mitigation of dental caries must be determined only on the basis of results obtained from clinical studies.

Using the Hanke (31) method for measuring the bactericidal effectiveness of antiseptics intended for use in the oral cavity, Shelton and Huyck (32) found that a solution containing 0.025 per cent (1:4000) cetylpyridinium chloride in a base of 18 per cent alcohol,

10 per cent glycerin and about 70 per cent distilled water gave a bactericidal efficiency of 90.64 per cent in an average of twenty-one cases after a period of three hours. The effectiveness of this solution after three hours was greater than the effectiveness reported by Hanke (31) for the National Formulary Antiseptic Solution after one hour, 3 per cent hydrogen peroxide after two hours and two well known organic mercurial germicides after two hours.

Assay

Auerbach (33) developed a colorimetric assay method for the estimation of some germicidal quaternary compounds including cetylpyridinium chloride in dilute solution. The method was found to be practical and specific since inorganic alkalies and primary, secondary and tertiary amines did not interfere. An extension of this general method was suggested for the estimation of alkaloids using bromothymol as indicator and for the estimation of some colored sulfonic acids.

Using the bromphenol blue colorimetric method of assay Munson (34) studied the effect of alkalinity on the assay of cetylpyridinium chloride and found that within the pH range of 7.49 and 10.07 the assay values gradually decreased. Two and thirteen hundredths moles of cetylpyridinium chloride were found to react with one mole of bromphenol blue. The Fischer Electrophotometer was not found to be as suitable as the Beckman spectrophotometer for measuring color intensities in this range. With the Beckman spectrophotometer set at 590 mμ, the concentration of cetylpyridinium chloride was determined by reference to a standard curve obtained by plotting color intensities against color intensities produced by known concentration of the germicide.

Summary

1. The physical properties, compatibilities and incompatibilities of cetylpyridinium chloride are discussed.

2. A review of the literature on cetylpyridinium chloride is presented with special reference to mode of action, relationship of chemical constitution to germicidal action, bacteriological action, pharmacological action, disinfecting action, action in the mouth and assay.

REFERENCES

1. Jacobs, W. A.: *J. Exper. Med. 23*:563-568 (1916).
2. Jacobs, W. A., Heidelburger, M., and Amoss, H. L.: *J. Exper. Med. 23*:569-576 (1916).
3. Jacobs, W. A., Heidelburger, M., and Bull, C. G.: *J. Exper. Med. 23*:577-599 (1916).
4. Powney, J.: *Nature 152*:76 (1943).
5. Anon.: *Soap and Sanitary Chemicals 18*:59 (June, 1942).
6. Frobisher, M.: *J. Infect. Dis. 38*:66 (1926).
7. Baker, Z., Harrison, R. W., and Miller, B. F.; *J. Expt. Med. 73*:249 (1941).
8. Albert, A.: *Lancet 2*:6222 (1942).
9. Shelton, R. S., Van Campen, M. G., and Nisonger, L. L.: Correlation of Structure and Germicidal Activity of Certain Acyclic Quaternary Ammonium Salts, Boston Meeting, American Chemical Society, September 11-15, 1939.
10. Shelton, R. S., Van Campen, M. G., Tilford, C. H., and Nisonger, L. L.: Correlation of Structure and Germicidal Activity of Some Quaternary Ammonium Salts derived from Cyclic Amines, Cincinnati Meeting, American Chemical Society, April 8-12, 1940.
11. Blubaugh, L. V., Botts, C. W., and Gerwe, E.: *J. Bact. 39*:51 (1940).
12. Miller, B. F., and Baker, Z.: *Science 91*:624-625 (1940).
13. Blubaugh, L. V., Gerwe, E. G., Botts, C. W., and Helwig, H. L.: *J. Bact. 41*:34 (1941).
14. Gershenfeld, L., and Milanick, V. E.: *Am. J. Pharm. 113*:306-326 (1941).
15. Green, T. W., and Birkeland, J. M.: *J. Bact. 41*:34 (1941).
16. Clarke, G. E.: *Urol. & Cutan. Rev. 46*:245-246 (1942).
17. Ordal, E. J., and Borg, A. F.: *Proc. Soc. Exper. Biol. & Med. 50*:332-336 (1942).
18. Kolloff, H. G., Wyss, A. P., Himelick, R. E., and Mantele, F.: *J. Am. Pharm. A. (Scient. Ed.) 31*:51-53 (1942).
19. Reed, G. S., Blubaugh, L. V., and Gerwe, E. G.: *J. Bact. 45*:43 (1943).
20. Blubaugh, L. V., *et al.*: Unpublished studies on the germicidal properties of cetylpyridinium chloride.
21. Warren, M. R., Becker, T. J., Marsh, D. G., and Shelton, R. S.: *J. Pharmacol. & Exper. Therap. 74*:401-408 (1942).
22. Sarber, R. W.: *J. Pharmacol. & Exper. Therap. 75*:277-281 (1942).
23. Green, T. W., and Birkeland, J. M.: *Proc. Soc. Exper. Biol. & Med. 51*:55-56 (1942).
24. Wakelin, J.: *Mfg. Chemist 10*:17-19 (1939).
25. Barnes, J. M.: *Lancet 1*:531-532 (1042).
26. Williams, R., Clayton-Cooper, B., Duncan, J. McK., and Miles, E. M.: *Lancet 1*:522-526 (1943).
27. Miller, B. F., Baker, Z., and Harrison, R. W.: *Proc. Soc. Exper. Biol. & Med. 42*:705-706 (1939).
28. Domagk, G.: *Deutsche med. Wchnschr. 61*:829-832 (1935).
29. Miller, B. F.: *Proc. Soc. Exper. Biol. & Med. 39*:389-393 (1938).
30. Miller, B. F., Muntz, J. A., and Bradel, S.: *Proc. Soc. Exper. Biol. & Med. 45*:104-108 (1940).
31. Hanke, M. T.: *J. Am. Dent. A. 27*:1379-1393 (1940).
32. Shelton, R. S., and Huyck, C. L.: Unpublished report on studies relating to cetylpyridinium chloride as an agent for gargle.
33. Auerbach, M. E.: *Ind. Eng. Chem. Analytical Edition 15*:492 (1943).
34. Munson, P. L.: Unpublished report on studies relating to the assay of cetylpyridinium chloride.

GLYCERINE KEEPS PACE WITH PHARMACEUTICAL PROGRESS

By Georgia Leffingwell, Ph. D., and Milton A. Lesser, B. Sc.

IT is not generally appreciated that one of the main reasons for glycerine's civilian-use curtailment was the fact that so much of this fluid went into medical supplies for the armed forces. This is quite evident in a report issued by the Division of Information of the War Production Board (1), which points out that, in addition to its other numerous and important war uses, in the Army, glycerine compounds rank second only to alcohol as solvents for medical solutions. "In pure form," said the report, "glycerine is a powerful antiseptic, used in many types of surgical dressings." Its value for its "highly effective emollient action" in dermatological conditions was also brought out, as well as its other uses for both the physician and the dentist.

Now that glycerine is again available to pharmacists and drug manufacturers in practically normal quantities, it is well to look back and see what has been learned during the brief period of necessary curtailment. A check of happenings during this time reveals certain definite facts. First, that glycerine is a basic, essential material in pharmacy and medicine. Changes made in official glycerine-containing preparations were recognized as but temporary expedients and were stated as such in the projected changes. Second, that no fully satisfactory substitute for glycerine has been found. Third, that continued developments in pharmacy and medicine continue to utilize glycerine in many new ways.

Glycerine is a major essential of so many pharmaceutical preparations, because it offers such an extensive combination of physical characteristics. These have been reviewed by several authorities during recent months. Merrill (2), for example, listed some of the important uses for glycerine as follows: (a) humectant, (b) vehicle, (c) solvent, (d) sweetening agent, (e) emollient, (f) reactive material, (g) lubricant, (h) softening agent, (i) penetrant, and (j) antifreeze agent. To this might well be added the observations made by

Prinz (3) in Canada. This authority pointed out that among glycerine's several functions in pharmaceutical preparations, the following are among the most important: (a) to give a certain "body" or viscosity to liquid preparations, (b) to prevent enzymic decomposition, particularly fermentation, of liquid preparations, (c) to act as a solvent for certain drugs; and, (d) to prevent the drying out of ointments, creams and pastes made with water.

In any discussion of its properties, one cannot omit the fact that glycerine, unlike many other solvents, is safe to use both in oral preparations and those intended for external, topical application. Indeed the importance of this characteristic was made quite evident when it became necessary for the government (4) as well as other interested groups (5), to issue warnings against the dangers of materials suggested as glycerine substitutes. These groups stressed the necessity for thorough investigation of all suggested glycerine substitutes.

Work done during the last year or two has shown that, while certain individual properties of glycerine could be duplicated, there was no single substance capable of giving the all-over characteristics inherent in glycerine. Some substances which might have served in certain instances are far too toxic for medicinal use (4, 5). British studies (6) have shown that whatever other virtues they may possess, the mucilage type of glycerine substitutes possess none of the water-holding properties peculiar to glycerine and other hygroscopic materials. In his discussion of the subject, Prinz (3) reported that, as a solvent, glycerine is difficult to replace and he warned that it would be wise to reserve some glycerine for such cases where no other solvent would serve. Speaking as a cosmetician, de Navarre (7) pointed out that spreading and plasticizing properties of glycerine would be most difficult to replace. The spreading effect, he noted, is particularly noticeable in vanishing creams which roll unless there is a sufficient amount of glycerine present. This fact becomes quite pertinent when it is realized that vanishing cream bases (e. g. "washable," greaseless ointment bases) are finding ever-widening utility in topical medication for the treatment of dermatological conditions, infections, wounds and burns.

All of these observations help to explain why glycerine is a premier material of pharmacy and medicine. Nowhere is this more apparent than in sulfonamide-containing preparations for external use.

The role played by glycerine was well evident in the recent report of the Council on Pharmacy and Chemistry of the American Medical Association (8) on the local use of sulfonamide compounds in dermatology. The following quotation from this important report is quite indicative: "What type of vehicle should be used for exhibiting these compounds? Unfortunately the sulfonamides are hardly soluble in water, much more so in glycerine, and Lain notably employs sulfanilamide in such a super-saturated solution on gauze, claiming excellent results. Kalz and Prinz have used a glycerine emulsion for their work. It has been clearly brought out by Pillsbury, Livingood and his co-workers, Prinz and Kalz, and others that greasy bases are unsatisfactory for applying sulfonamide locally. A grease will seal off the area, it does not mix with serum, and it may coat over the underlying infection and furnish an anaerobic pocket in which the infection may thrive. Moreover, bacteria covered with a film of grease will not be so easily reached by the medicament. Oil-in-water emulsion bases provide a more satisfactory medium than vanishing cream compounds and are apparently the best bases for applying any of the sulfonamides."

The glycerine-containing oil-in-water emulsion type base, developed by Pillsbury and his collaborators (9), used as an example in the A. M. A. report, is as follows:

Sulfathiazole	5.0 per cent
Sodium lauryl sulfate	1.0 "
Stearyl alcohol	10.0 "
Cetyl alcohol	3.0 "
Spermaceti	10.0 "
Glycerine	10.0 "
Water	61.0 "

However, glycerine-containing sulfonamide compositions are not limited to the treatment of dermatological conditions, but find wide application in the therapy of burns, surgical wounds, accidental wounds and other disorders. For example, in his report on the use of a preparation consisting of 30 per cent of sulfathiazole in glycerine, Wood (10) found this simple combination effective in the treatment of such varied indications as: minor surgery, general surgery, leukorrhea, burns, osteomyelitis, tonsillectomy, preoperative skin preparation, and compound fractures.

Glycerine has a well-established role in sulfonamide-containing burn treating products. As these products are improved or modified, it is generally found that glycerine continues to serve its useful functions. During the last year or so, so-called "sulfa films" have come into increasing use for treating burns. These compounds contain substances which on drying form protective films over the injured area. Glycerine often serves as the plasticizer for these films to keep them pliable and flexible and to prevent their drying and cracking. An example of such usage is given in the report of Skinner and Waud (11) on a plastic film treatment of experimental burns. Two solutions were tested, these being made as follows:

Burn Fluid 19

Glycerine	80 Gm.
Triethanolamine	5 "
Urea	5 "
Sulfathiazole	5 "
Sulfanilamide	5 "
Stock solution of methyl cellulose	100 "
Stock solution of polyvinyl alcohol	800 "

Burn Fluid 20

Glycerine	40.0 Gm.
Triethanolamine	2.5 "
Urea	5.0 "
Phemerol	0.5 "
Sulfanilamide	5.0 "
Stock solution of polyvinyl alcohol	947.0 "

The stock solutions of the film-forming compounds were as follows:

Stock solution of methyl cellulose

Methocel 25 C. B. D.	8.0 per cent
Benzoic acid	0.1 "
Ringer's solution to	100.0 "

Stock solution of polyvinyl alcohol

Polyvinyl alcohol	8.0 per cent
Benzoic acid	0.1 "
Ringer's solution to	100.0 "

Studies of the results in two hundred and twenty-nine experimental burns on rabbits showed that burns treated with burn fluids 19 and 20 heal at least five days before tannic acid treated burns, ten days before burns treated with weak triple dye solution, and a full forty days before burns treated with strong triple dye solution. These burn fluids were easily applied and gave very satisfactory eschars. Moreover, they were smooth and pliable, and being water-soluble, were readily removed after soaking for a few minutes in warm saline.

However, the usefulness of glycerine extends to most types of burn preparations including those based upon tannic acid, dyes, silver nitrate, as well as the sulfonamides (12). The role of glycerine in tannic acid burn jellies, though long well established was fully confirmed in its importance by the extensive studies of Tomski (13) in England. Indeed, as newer materials are adapted or suggested for burn therapy, glycerine is often concurrently advocated as an essential conjunct. Thus in a patent (14) covering the use of tannic acid and polyisobutylene as the two main ingredients of a creamy emulsion for applications, it was advocated that from 5 to 10 per cent of glycerine be included as a hygroscopic and softening agent to prevent the development of a harsh or unduly stiff coating.

As a matter of fact, sterile glycerine, by itself, is finding important application in the treatment of burns, more especially burns of the hands and face where tough eschar formation is not desirable (15).

Although glycerine has not been much associated with the new patent antibacterial agent, penicillin, there are indications that it may be of some value in the use of this drug. As is well known, pure penicillin is limited to the needs of the armed forces. However, it occurred to Robinson and Wallace (16) that the direct application of a less pure product might be of advantage in the local treatment of wounds, furunculosis, sinus infections, gonorrhea, and other infections of the skin or mucous membranes. To produce the penicillin in contact with the lesions, they placed a gauze dressing in a Petri dish and saturated it with a medium containing 1 per cent yeast extract, 2 per cent dextrose, 2 per cent cornstarch and 2 per cent glycerine. This was sterilized by autoclaving and inoculated with penicillium.

It was found that a fair amount of penicillin was produced after four or five days and that a bacteriostatic condition would be maintained at the point of contact with the lesion. Clinical application of

the penicillin dressing was made on a series of patients who had not been relieved by other forms of therapy. Results on a small series of patients were most encouraging and indicated much promise for the method.

For many years glycerine has found many applications in the prophylaxis and treatment of allergic conditions. Among its most important uses is its employment as an extractive and vehicle for production of allergenic preparations used for testing or reducing sensitivity to various exciting substances (17, 18). Asthma, one of the more unpleasant sequels of allergic disorders, is also treated and paroxysms made less severe by the use of glycerine-containing compounds, many of them developed during the last year or so. This is especially true of new inhalants for the relief of asthmatic attacks. These inhalants, applied by means of an atomizer to provide a fine spray to afford relief of asthmatic coughing, wheezing and choking, are usually based upon the use of epinephrine (adrenalin, suprarenalin, etc.).

However, epinephrine by itself has certain undesirable effects such as lack of stability in solution, short duration of action, irritative effects on the nose and throat, and undesired systemic side-effects. Various methods had been advocated to overcome these disadvantages. In 1942, Cole (19) advocated the use of the following glycerine-containing solution prior to an asthmatic attack:

Methyl atropine nitrate or bromide	0.14 per cent
Papaverine	0.08 "
Sodium nitrate	0.08 "
Adrenalin	0.05 "
Lactic acid	2.50 "
Glycerine	10.00 "
Distilled water, to make	100.00 "

More recently, Lockey (20) suggested another method for improving these inhalant sprays by the addition of glycerine. He had found that epinephrine-induced dryness of the throat will often disappear if the patient swallows a little glycerine immediately after inhaling the spray. He therefore prepared the following solution:

Suprarenalin crystals	10.0 Gm.
Sodium chloride	9.0 "
Chlorobutanol	5.0 "
Sodium bisulfite	0.9 "
Dilute hydrochloric acid	20.0 cc.
Glycerine	50.0 cc.
Distilled water, to make	1000.0 cc.

Carefully controlled clinical tests with this preparation showed that irritation and dryness of the throat appeared 82 per cent less frequently in the group which used the glycerized solution. Longer periods of relief were obtained also, and most patients expectorated more frequently and productively.

Other recent developments involving the use of glycerine further illustrate the versatility of this fluid. One example will suffice to show this fact. Back in 1941, a combination of equal parts of phenol and camphor was suggested for the treatment of "athlete's foot." Subsequent reports indicated that this mixture was dangerously caustic, especially when applied to wet surfaces. However, Verhoeff (23) has prepared a glycerized mixture that also contains phenol and which it is claimed is harmless even when applied to wet skin. The formula is as follows:

Phenol crystals (melted)	2 cc.
Ethyl alcohol (95 per cent)	2 cc.
Glycerine	4 cc.

The solution is applied by thoroughly rubbing the affected region with the end of the finger; application being made twice daily, or once daily in mild cases. It is most effective immediately after the feet and lesions have been washed with soap and water. After healing, an application once a week is to be continued to prevent reinfection. Healing is rapid; about a week in mild cases, in three weeks in more severe cases. Despite the report that this composition is harmless, it is evident that any preparation with so high a proportion of phenol should be used only under a physician's direction.

From the foregoing it is evident that glycerine is one of the most useful of medicinal and pharmaceutical materials—one that cannot be dispensed with. These few instances (and many more could be cited) merely serve to show that glycerine is continuously assisting and accelerating the pace of medical progress.

BIBLIOGRAPHY

(1) Division of Information: "Glycerine Report", Washington, W. P. B.-3363, April, 1943.

(2) Merrill, E. C.: (Through) *Oil, Paint & Drug Reptr.*, May 17, 1943; also, *Drug Trade News*, May 7, 1943.

(3) Prinz, M. V. H.: *Canadian Pharm. J.*, March 1, 1942, p. 124.

(4) Capps, R. W.: Official Notice, U. S. Dept. Agric., Food Distribution Administration, Fats and Oils Branch, Washington,, April 6, 1943.

(5) Scientific Advisory Committee: Toilet Goods Assn., Bulletin 549, March 24, 1943.

(6) Atkins, F.: *Pharm. J. 151*:122 (1943).

(7) de Navarre, M. G.: *Am. Perf. & Essent. Oil Rev.*, April, 1943, p. 27.

(8) Cole, H. N.: *J. A. M. A. 123*:411 (1943).

(9) Pillsbury, D. M., Wammock, V. S., Livingood, C. S., and Nichols, A. C.: *Am. J. Med. Sci. 202*:808 (1941).

(10) Wood, E. H.: *Clin. Med. 50*:231 (1943).

(11) Skinner, H. G., and Waud, R. A.: *Canadian M. A. J. 48*:13 (1943).

(12) Dept. of Health for Scotland: E. M. S. Memorandum No. 8 (through) Pharm. J.

(13) Tomski, H. W.: *Pharm. J. 146*:276 (1941); *143*:11 (1941).

(14) Holmes, R. L., and De Hoff, H. C.: U. S. Pat. 2,312,715, March 2, 1943.

(15) MacKenzie, W. C.: *Canadian M. A. J. 47*:443 (1942).

(16) Robinson, G. H., and Wallace, J. E.: *Science 98*:329 (1943).

(17) Cohen, M. B.: *J. Allergy 10*:470 (1939).

(18) Unger, L.: *J. Allergy 13*:326 (1942).

(19) Cole, L.: *Practitioner 148*:204 (1942).

(20) Lockey, S. D.: *J. Allergy 14*:382 (1943).

(21) Verhoeff, F. H.: *New England J. Med.*, August 12, 1943.

ECONOMIC REALITIES

SPENDING POWER VERSUS BUYING POWER

By Karl Scholz, Ph. D.*

MONEY spending power is popularly used interchangeably with money buying power. But a moment's reflection should make us realize that spending power is the ability to give up something we have, for something else we would like to have. On the other hand, buying power is our ability to get something that we would like to have, for something we have to give up.

Money buying power and spending power would be essentially the same, if a dollar we have to spend would continue to buy the same average amount of goods of constant quality. Under such conditions, if a person received more dollars to spend, he would also be able to buy correspondingly more goods with these dollars. But if he receives more dollars and prices rise proportionately, he will have no more real buying power, even though his money spending power will have increased.

One reason for the confusion of money spending power with the buying power of money is due to the fact that we ordinarily relate the buying power of money to a unit quantity, such as the dollar. Thus we speak of changes in the buying power of the dollar, when prices, expressed in dollars, either rise or fall. On the other hand, we think of spending power in terms of the number of dollars which we actually have in our possession or control. Therefore, the more dollars we have, the greater will be our money spending power.

The proprietor of a restaurant does not speak of buying a dollar for a meal, but the customer, who has a dollar, thinks in terms of buying a meal for a dollar. To him his money spending power is the same as its buying power. So long as he can get a meal for his dollar, he appears to be satisfied if he has the dollar. He would no doubt be somewhat disillusioned if no one would either be able or willing to sell him a meal for a dollar, or possibly give him only a plate of soup for it.

---

* Professor of Economics, University of Pennsylvania.

All this may sound rather academic and unrealistic. Yet an understanding of the difference between monetary spending power and its real buying power, i. e. the ability to get goods for one's money, is rather important, if we would face economic realities.

All out production for total war has increased the money spending power received by the people by leaps and bounds in recent years. This money spending power finds expression, in the first instance, in the form of national income paid out. This national income, in the form of wages and salaries, interest rent and profits totalled 70.7 billion dollars in 1939, while in 1943 it had more than doubled, to an estimated 142 billion dollars. At the end of 1943 money income was being paid out at an annual rate of over 150 billion dollars. In 1939, around 44.5 billion dollars or 62.7% of the national income was received in the form of wages and salaries. On the other hand, wages and salaries absorbed approximately 72.5% of the total income paid out in 1943.

The total money spending power received by the wage earners of the United States has thus more than doubled during the past five years. But the real buying power of every dollar of this money spending power has already decreased by some 20 to 25% since 1939, due to the rise in the cost of living. Moreover the buying power of dollars is also being restricted for the duration because of the shrinkage in the supply of saleable civilian goods. If it were not for wartime price controls and rationing, we would soon discover that the increasing money incomes, resulting from war production, would lose some of their real buying power, through rapidly rising prices of the relatively scarce supply of various consumers' goods. Nor could such a deficiency of real buying power be removed by increasing money spending power in the form of higher wages and salaries or increased property incomes.

In spite of ever heavier Federal taxes to finance the war program, and increased purchases of war bonds out of current income, the money spending power remaining in the hands of the people and in bank deposits totals many billions of dollars. This money would soon lose much of its real buying power, if it were used to bid for the available supply of consumers' goods.

If at the close of the war there should be a rush to buy the things we are denying ourselves for the duration, we would likewise discover, that in the absence of continued government price controls

and rationing, the buying power of our wartime money accumulations would decline rapidly.

If therefore we would seek to protect the buying power of every dollar of our accumulating money spending power, we must continue to exercise a large degree of thrift and restraint after the war even as we are being urged to do during the war. Not until our industries have been reconverted to peace-time production, and produce efficiently and economically at low unit costs, may we hope to reap some of the benefits of our wartime money accumulations. We should not lose sight of the fact that a war boom is essentially a money boom, rather than an ordinary business boom, with an oversupply of saleable goods.

It will require much hard labor and many dollars of invested savings after the war to accomplish reconversion of our economy to a peace-time basis. Patience and continued thrift will have to become real virtues of consumers, if they would derive any benefits after the war from their wartime accumulations of monetary spending power. But at best, they will probably discover that some of the buying power of their money will disappear in the form of higher costs of living than those which prevailed before the war.

SCHERING ANNOUNCES NEW ESTROGEN

A new orally effective estrogenic substance, ethinyl estradiol, has been announced by the Schering Corporation. It will be sold under the name "Estinyl." This new estrogen is five to twenty times as potent as Stilbestrol when given by mouth and it is claimed that it is less toxic. Estinyl Tablets are available in two strengths, 0.02 mg. and 0.05 mg., in bottles of 30, 60 and 250 tablets.

SELECTED ABSTRACTS

A Study of American Musk From Muskrats. Editorial Staff of Givaudan-Delawanna, Inc., P. G. Stevens and J. L. E. Erickson. *Am. Perfumer 45,* No. 12, 35 (1943). For many years the fixatives used in the perfume industry have been the following: musk, which consists of the dried secretion of the preputial follicle of the muskdeer of Tibet and China; civet, a glandular secretion of the Abyssinian civet cat; castoreum, obtained from the beaver of Siberia and northern Canada; and ambergris, from the sperm whale.

In 1942 Stevens and Erickson announced the isolation from the scent glands of the Louisiana muskrat a mixture consisting of 98 per cent of two cyclic alcohols and 2 per cent of their corresponding ketones. These compounds possessed a ring structure containing respectively 15 and 17 carbon atoms; accordingly, the alcohols were designated cyclopentadecanol (nor-muscol) and cycloheptadecanol (dihydrocivetol) and the ketones cyclopentadecanone and cycloheptadecanone.

The average weight of the scent gland from the male muskrat is about 1.5 grams; since that of the female weighs only one-fourth that amount it is impractical to collect the latter. The glands were shipped in metal containers half filled with ethyl or isopropyl alcohol.

For the process of extraction the glands were drained free of alcohol, washed with ether, comminuted, and extracted with ether in a Soxhlet apparatus. The ethereal extract was combined with the alcohol used as preservative and the wash ether; the evaporation of the solvents used to treat from 800 to 1000 musk glands yielded a crude musk extract weighing 10 ounces.

Saponification of the extract with 10 per cent alcoholic potassium hydroxide solution permitted the separation of acid and neutral portions. The latter fraction, after removal by shaking out with ether and evaporation of the solvent, yielded about three ounces of a neutral musk oil. The portion of this material distilling at 130-170°/1 mm. solidified to one ounce of a waxy substance with a fine musk odor. It was saturated toward bromine, and it possessed only slight optical activity.

By vacuum fractionation this substance was shown to be a mixture of 58 per cent of dihydrocivetol (C_{17}), 40 per cent of nor-muscol (C_{15}), and two per cent of the corresponding ketones.

By chromic acid oxidation the two musk alcohols were converted to their respective ketones, in which alone reside the desired odor and fixative qualities.

The ketones obtained from muskrat musk are closely related to the odoriferous principles muscone or 3-methyl-cyclopentadecanone (from muskdeer musk) and civetone or 9-cycloheptadecanone (from civet).

Civetone occurs in civet to the extent of three per cent; the corresponding alcohol civetol and skatole (β-methyl-indole) are also found in this material. Ruzicka discovered in 1929 that the yield of civetone could be increased by oxidation of the alcohol.

The odoriferous constituents of castoreum were studied in 1927 by Walbaum and Rosenthal and also by St. Pfau. They consist largely of aromatic compounds, among which were isolated acetophenone, benzyl alcohol and various phenols. No compounds containing large rings were present.

Autoxidation Impurities in Ethyl Alcohol. A. E. A. Werner. *Analyst, 68,* 365 (1943). A recently purchased specimen of alcohol obtained from molasses was found to possess an unpleasant odor, although conforming to B. P. tests. Comparative tests were carried out on this sample and on alcohol obtained from grain and potatoes in order to study the formation of aldehydes and peroxides.

Tests for aldehydes were performed by adding 1 ml. of Schiff's reagent to a dilution of 2 ml. of each sample and 7 ml. of water. A purple-red color, developing to its maximum intensity in fifteen minutes, was observed with the samples from molasses and potatoes, being much more pronounced in the case of the former; grain alcohol gave negative results. It is necessary to dilute the samples of alcohol with water in performing this test, since grain alcohol develops a color which is apparently due to some change in Schiff's reagent and not to the presence of aldehydes.

Each of the alcohols was examined for peroxides by adding 5 ml. of a 2 per cent ammonium thiocyanate solution to a 2 ml. sample, followed by a crystal of ferrous sulfate. The molasses alcohol rapidly developed a blood-red color, and the potato alcohol gave a weak positive reaction. The grain alcohol gave a negative reaction.

That the development of aldehydes and peroxides is due to a process of autoxidation was shown by exposing samples of the alcohols to sunlight for three months. Another sample of the molasses

alcohol was preserved in the dark as a control; to another sample of this product exposed to sunlight were added a few crystals of ferrous sulfate as a catalyst.

At intervals of one month the aldehyde and peroxide concentrations were estimated colorimetrically by comparison with the control. Autoxidation was most pronounced in the case of the molasses alcohol, but it was completely absent in the case of grain alcohol. Potato alcohol was intermediate in position. Ferrous sulfate greatly catalyzed the development of aldehydes in molasses alcohol; the small amount of peroxides formed decomposed within one month, and were absent in subsequent examinations.

It is believed that autoxidation in alcohol obtained from molasses and potatoes is induced by a small amount of some impurity which is not removable by distillation.

CTAB: Cetyl-Trimethyl-Ammonium Bromide. T. D. Whittet. *Chem. Products*, 7, No. 1-2, 8 (1943). This cationic detergent, now available under the brand name "Cetavlon," has the formula $C_{16}H_{33}(CH_3)_3$ N Br. It is offered as a 7.5 per cent W/W aqueous solution which has a translucent, soapy appearance; it is incompatible with soap and other anionic compounds and with proteins.

A crude product used in earlier investigations possessed a brown color and a distinctly fishy odor due to trimethylamine hydrobromide; this impurity is not present in the CTAB now available.

Barnes has shown that CTAB materially reduces the number of bacteria on the hands and that it is painless and harmless to raw surfaces. It is also effective in disinfecting bowls and baths which are too bulky to sterilize by heat.

Williams *et al.* have shown that it is superior to soap and water for cleansing and sterilizing the hands in pre-operative preparation for gloveless surgery. These authors found that only a very low percentage of persons exhibited any degree of sensitivity of the skin toward CTAB.

The author reports that both the crude and purified preparation have been used extensively for a year at the hospital with which he is connected and that no cases of skin reaction or sensitivity have been observed. The use of Cetavlon solution, diluted one in ten, is recommended for cleansing dirty and infected wounds. The addition of some dye such as eosin is suggested for the delineation of areas on the body when the detergent solution is used in pre-operative cleansing.

Pectin as an Emulsifying Agent. Harry Lotzkar and W. Dayton Maclay. *Ind. Eng. Chem. 35,* 1294 (1943). The comparative efficiencies of pectin, tragacanth, karaya and acacia as emulsifying agents have been investigated in a study of aqueous emulsions of olive oil, cottonseed oil and mineral oil. The effect of pH, oil-water ratio and concentration of agent was observed in respect to the interfacial surface of the dispersed oil and the viscosity of the product. There is little difference between pectin and tragacanth as emulsifying agents for olive oil; both are more effective at lower pH values. Pectin appears to have a slight advantage over tragacanth in cottonseed oil emulsions. It is superior to tragacanth and acacia, and at least equal to karaya, as an emulsifying agent for mineral oil.

Sulfadiazine in the Treatment of the Common Cold. R. E. Cecil, N. Plummer and W. G. Smillie. *J. A. M. A. 124,* 8 (1944). A series of 72 colds in 66 different persons was studied clinically and bacteriologically. Of these cases 48 received 3 grams of sulfadiazine daily by mouth for four days, while 24 served as controls.

At the start of treatment and every second or third day thereafter the following procedures were carried out: (1) oral temperature, (2) complete blood count on the patients receiving the drug, and hemoglobin determination on the controls, (3) record of symptoms with their intensity at the time of visit, (4) examination of the upper respiratory tract, and (5) nasopharyngeal culture. In addition, gross and miscroscopic urine examinations were made at the start of therapy, and later if they were indicated. The blood level of sulfadiazine was determined twice during the course of treatment.

The clinical findings failed to indicate that sulfadiazine appreciably shortens the duration of the common cold; in the controls the average time was 9.7 days, and in the treated group 8.1 days. However, following sulfadiazine therapy some diminution of the severity of symptoms was noted, due to control of secondary bacterial infection. There was also a uniform decrease in the total number of organisms present in the nasopharyngeal tract and a check in the growth of pathogens.

Sulfadiazine is considered to be the least toxic of the sulfonamides. No serious toxic reactions occurred during this study. Two cases displayed mild renal reactions: in one there was slight flank

pain, accompanied by many crystals in the urine; in the other there was mild pain in the lower part of the abdomen radiating to the scrotum, with a few red blood cells in the urine. Another patient showed a sudden drop in the leukocyte count upon the completion of therapy, but regained a normal count within a few days.

The authors oppose the routine use of the sulfonamides in the treatment of the common cold, and would restrict their use in this connection to selected cases as a protection against severe secondary infection.

Therapeutic Cure of Acute Experimental Toxoplasmosis in Animals. D. Weinman and R. Berne. *J. A. M. A. 124,* 6 (1944). Toxoplasmosis is almost invariably fatal in man, the principal cause of the failure of therapy probably being the short period in which the patients are available for treatment. Often only a few days elapse between the initial symptoms and death.

Sabin and Warren were the first investigators to demonstrate the effects of the sulfonamides on mice infected with this disease, but a study of their data suggested to the present authors that adequate blood levels of the drugs may not have been obtained.

To test this point Weinman and Berne studied the effects of sulfapyridine, sulfadiazine and sulfathiazole suspended in cottonseed oil and injected subcutaneously and of saline solutions of the first two sulfonamides injected intraperitoneally into mice infected with a toxoplasma strain isolated from guinea pigs.

The average survival period of untreated controls was fifteen days in one series and sixteen in another. In order to duplicate the conditions in which human patients become available for treatment, the mice used in the experiments received therapy late in the course of the infection.

It was found that when treatment was begun at the expiration of one-third of the expected survival period nearly all of the animals recovered. Only one-half of the mice survived if treatment was delayed beyond the end of the second third of this period. Sulfapyridine proved strikingly successful in curing the disease, even in extreme cases in which the drug was withheld until three days before death was expected. Trials with the other sulfonamides were not sufficiently extensive to permit definite conclusions.

It was found that infected mice which survived the disease remained carriers, retaining virulent organisms in the brain.

SOLID EXTRACTS

The expansion of penicillin production is taking place at an almost unbelieveable rate. The production during January was approximately 6000 per cent higher than in June, 1943. January production was 40 per cent over December. Although production is not yet adequate to supply civilian needs certain selected cases may be treated with an allocated portion of the carefully controlled supply.

AJP

Penicillin is probably not the only natural antibacterial substance that will find a place amongst the chemotherapeutic substances. Clavicin from Aspergillus clavatus and flavicin from Aspergillus flavatus have shown promising antibacterial properties. The use of patulin has also been widely publicized.

AJP

That the Drug and Cosmetic industries are making careful post-war plans is evident by a survey made by the Curtis Publishing Company of Philadelphia. Among those companies studied 62 per cent reported that they are planning new products for the post-war market. In other fields there seems to be a great tendency to invade other markets, e. g., an airplane company intends to manufacture farm implements, a plumbing and heating company aviation instruments, and a house-furnishings company boats!

AJP

The physiological reaction of the five senses to color under certain conditions has been looked into scientifically by the color research laboratory of the Eagle Printing Ink Company, division of G. P. I. When the ears are exposed to a loud noise, red colors grow dim, and green and blue become brighter, it is claimed.

The action of the eye to color while the sense of smell was being stimulated resulted in strong odors having a similar effect to loud noise, the eye being less sensitive to red and more sensitive to green.

AJP

A new filter material called multipore has been announced by the U. S. Rubber Co. In making the filter, rubber latex is spread on a cured rubber blanket containing about 6400 microscopic pits per square inch. When this is heated the air trapped in each pit is expanded thus blowing a hole through the film. The filter may be made of either hard or soft rubber and it may be compounded to resist abrasion, high temperatures, alkaline and acid solutions and certain oils and greases.

One of the paramount uses of this product is in the preparation and administration of blood plasma and whole blood as used in modern methods of transfusion. The filters serve to separate blood clots from whole blood, and "veils" or cloudiness which sometimes form in blood plasma.

AJP

The use of the sulfonamides in reducing the mortality of meningitis is strikingly shown by statistics. Before the use of sulfonamides 17 cases per 100 ended fatally; today only 3 per 100 are fatal. The spread of epidemic meningitis may also be effectively prevented by the use of prophylactic doses of sulfathiazole.

AJP

The oral administration of copious quantities of isotonic sodium lactate solution was recently reported as being of great value in the treatment of shock due to extensive burns. The simplicity of this treatment compared with intravenous therapy makes it most interesting and further clinical studies are being made.

AJP

Dr. F. J. Cullen of the Proprietary Association of America recently advised its members to be more truthful in the advertising claims for vitamins and to consider them only in the field of preventive medicine. He is to be complimented on this forthright stand since the public has already shown signs of revolt at some of the scare advertising in this field. If these excesses continue the current popular belief in the value of adequate nutrition and vitamin supply may be impaired.

BOOK REVIEW

Directory of Biological Laboratories. 2nd edition. 1943. 96 pages. Burns Compiling and Research Organization. Chicago, Illinois. $3.00.

Approximately 800 biological laboratories of the United States, including research, consulting and commercial, and those related to manufacturing processes, the latter embracing food and nutrition products, vitamin products, organic chemicals and pharmaceuticals, biologicals, glandular products, etc., are listed in this book.

The name and street address are given along with the professional functions and the scope of the activities. So far as possible it includes the name of the director in charge and designates the business office that purchases materials, supplies and equipment. Included as a biological laboratory is any laboratory which is professionally concerned with biological, bacteriological, serological or biochemical investigations, omitting exclusively clinical laboratories, also omitting colleges. In addition the Buyer's Guide lists manufacturers and distributors of materials, supplies, apparatus and equipment. It is classified as to products and completely cross-indexed. It shows sources of supply for all items used in biological laboratories and a complete where-to-buy-it information accurately classified.

It is indispensable for personal use, office reference, salesmen and sales departments, professional reference, checking mailing lists, and the technical library.

M. O. H.

PROFESSIONALLY DISTRIBUTED VITAMINS

You won't find NATOLA* or ABDOL* in a bin at the supermarket or next to the soap counter at the corner grocery. The PARKE-DAVIS vitamin line is *professionally distributed* . . . detailed to physicians and sold only through pharmacists.

Fifty-six per cent of those who buy vitamin products buy them on the advice or prescription of a physician . . . and he expects you to dispense a *professional* product, as distinguished from the products he sees featured in the grocery.

If you wish to retain your share of the *professional* vitamin market,—detail, display, and sell a *professional line* of vitamin products . . . the PARKE-DAVIS line.

*Trade-Marks Reg. U.S. Pat. Off.

ARMY E NAVY

PARKE, DAVIS & COMPANY

DETROIT, MICHIGAN

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.	Covers with Titles
50 copies.....	$3.50	$6.00	$10.50	$11.25	50 copies $5.00
100 "	4.25	7.00	14.00	15.00	100 " 6.50
250 "	5.25	9.00	18.75	20.00	250 " 10.25